

## Development and manufacturing of a biobetter therapeutic: A case study

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Activated Protein C (APC) is a naturally occurring human protease that has both anticoagulant and cytoprotective activities, with the latter being appropriate for treatment of ischemic stroke. ZZ Biotech has created a variant, 3K3A-APC, which reduces the anticoagulant activity while retaining its cytoprotective activity, thereby avoiding the dose-limiting side effect of unwanted bleeding. We describe the development of recombinant CHO-cell production and purification of 3K3A-APC, from small cultures to 2000-liter production. By working collaboratively, scientists from both companies were able to overcome this molecule's challenges of complex post-translational modifications, enzyme isomers, and autodigestion. The result was a successful regulatory filing leading to a Phase 1 clinical trial, which recently completed.

### Biography

Michiel E. Ultee, Ph.D., has more than 25 years of experience in the biopharmaceutical industry and has worked with antibodies since 1975. He serves as Laureate Biopharma's scientific head and is the leader behind Laureate's Scientific Series, which spotlights the organization's strategies and methods in working together with our clients' scientists to overcome challenges in biopharmaceutical development and manufacturing their biopharmaceutical products. He has been part of Laureate's biopharmaceutical operations team since 1987 with positions including Vice President of Process Sciences and Director of Manufacturing & Technical Operations. He is a frequent speaker at biopharmaceutical conferences, and a member of the editorial advisory boards of *Bioprocess International* and *Biopharm International*.

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